PATENT
Customer No. 22,852
Attorney Docket No. 1975.0025

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re PCT Application PCT/EP98/08522 of:	)	
	)	
Rudi BRANDS	)	Group Art Unit: 1648
	)	
U.S. Application No.: 09/582,342	)	Examiner: B. Li
	)	
PCT Filed: December 17, 1998	)	
	)	
National Stage Entered: June 23, 2000	)	
	)	
§ 371 Date: September 18, 2000	)	
	)	
For: PREPARATION OF CELLS FOR PRODUCTION OF BIOLOGICALS	)	

Mail Stop Appeal Brief - Patents

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

APPEAL BRIEF UNDER 37 C.F.R. § 1.192

In support of the Notice of Appeal filed June 11, 2003, and pursuant to 37 C.F.R. § 1.192, Appellants present three copies of their brief on appeal, and a check in the amount of $2340.00 covering the $330.00 fee under 37 C.F.R. § 1.17(c), and the $2010.00 fee for the accompanying Petition for Extension of Time (Five Months).

Please grant any additional extensions of time required to enter this Appeal Brief and charge any additional required fees to our Deposit Account No. 06-0916.

I. Real Party in Interest

The real party in interest is Duphar International Research B.V., Assignee of the present application.

II. Related Appeals and Interferences

To the best of the undersigned's knowledge, there are no related appeals or interferences known to Appellant, the Appellant's legal representative, or Assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

III. Status Of Claims

Claims 1, 2, and 7-26, as amended, are currently pending. Claim 1 is independent. The remaining claims have been cancelled without prejudice or disclaimer.

IV. Status Of Amendments

The Amendment filed December 20, 2002, has been entered. Appendix A presents the claims in the form pending after entry of that Amendment.

V. Summary Of Invention

Appellant has discovered and claims discontinuous methods for preparing cells for the manufacture of a biological. *See* specification at page 1, lines 4-5; *see also id.* at page 2, lines 1-15. The skilled artisan practicing an embodiment of the claimed methods cultures cells to produce a preproduction batch, and then divides the cells of

the preproduction batch into two parts. *Id.* at page 2, lines 1-15. The artisan uses the cells of the first part to prepare a culture of cells to grow a biological such as a virus for a vaccine. Accordingly, this first part forms a "production batch." *Id.* at page 2, lines 4-5 and 27-28. The artisan employs the cells of the second part to seed at least one additional batch that will not be used for the production of any biological product. This additional batch thus is known as a "subsequent preproduction batch." *Id.* at page 2, lines 6-7 and 30-32. The cells of the subsequent preproduction batch can be expanded to a greater cell population, if the artisan so chooses, before a production batch is prepared from the subsequent preproduction batch. *See, e.g., id.* at page 6, lines 15-16. These actions may, moreover, be repeated. *Id.* at page 2, line 3.

These methods depart from the alleged prior art because the skilled artisan practicing the claimed invention cultures subsequent preproduction batches and production batches from the same preproduction batch. This allows, potentially, the skilled artisan to culture subsequent preproduction batches and production batches at the same time. Using this approach, a vaccine manufacturer, for example, can rapidly produce vaccine without waiting for all preproduction batches to reach full maturity. *See* specification at page 3, line 35 to page 4, line 2. A description of Appellant's approach cannot be derived from the disclosure of the alleged prior art.

VI. Issue

Whether claims 1, 2, and 7-26 are non-obvious and patentable under 35 U.S.C. § 103(a) over *Griffiths et al.* (BRYAN GRIFFITHS & DENIS LOOBY, *Scale-Up of Suspension and Anchorage-Dependent Animal Cells, in* 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS 59 (Jeffrey W. Pollard & John M. Walker eds., 2d ed. 1997))

and[1] *Pollard* (JEFFREY W. POLLARD, *Basic Cell Culture, in* 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS 1 (Jeffrey W. Pollard & John M. Walker eds., 2d ed. 1997)).

VII. Grouping Of Claims

Claims 1, 2, and 7-26 stand or fall together.

VIII. Argument

Claims 1, 2, and 7-26 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over *Griffiths et al.* and *Pollard*. Final Office Action dated March 11, 2003, at page 2. Allegedly, "Griffiths et al. and Pollard teach all aspects of scale-up culturing suspension and anchorage dependent cell culture, unless the exactly split the preproduction of cell population into two parts, which is noticed by Office as a modification of splitting cells in different ratios." *Id.* at page 3. Moreover, "the discovering the workable ranges as 1 to 1 or 1 to 2 splitting cells in culture involves only routine skill in the art." *Id.* at page 4. From this, the Examiner concludes, "Unless there is [an] unexpected result by dividing the culturing cells into two parts compared with dividing cells into three part five parts, the rejection is maintained since the claimed invention as a whole is prima facie obvious absence unexpected results[.]" *Id.*

Appellant respectfully asserts that this logic reveals a complete misunderstanding of the

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[1] The Examiner poses the rejection in terms of "[*Griffiths et al.*] and [*Pollard*]." *See* Final Office Action at page 2 (emphasis added). Appellant understands this to signify the more conventional "[*Griffiths et al.*] in view of [*Pollard*]." Nonetheless, Appellant addresses the rejection as resting on the disclosures of these documents both individually and in combination.

claimed invention and the prior art. Accordingly, Appellant requests that the rejection be reversed.

A. One Rejection Remains

"Please note any ground of rejection(s) that has not been repeated is removed." Final Office Action at page 2. Accordingly, Appellant addresses the only rejection set forth in the Final Office Action, which is the rejection of claims 1, 2, and 7-26 under 35 U.S.C. § 103(a) over *Griffiths et al.* and *Pollard*. *Id.* Since the Examiner maintains the obviousness rejection "on the same ground as stated in the previous Office Action" (*id.*), Appellant addresses the rejection over *Griffiths et al.* and *Pollard* where it appears throughout the prosecution history. *See* Office Action mailed on August 1, 2001, at pages 3-4; Advisory Action mailed on December 3, 2001, at pages 2-3; Office Action mailed on September 20, 2002, at pages 4-5.

B. Cited Documents May Have Been Received by Public by August 27, 1997

Further to the discussion of the publication date of *Griffiths et al.* and *Pollard* found on pages 2 and 3 of the Final Office Action, the Examiner has provided a photocopy of the preface of 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS, second edition, which shows a marking appearing to read "8/27/97." *See* facsimile from Examiner Li to Jeremy Stipkala dated June 10, 2003, at page 3. Appellant concedes, for the purpose of this appeal to the Board only, that *Griffiths et al.* and *Pollard* may have been received by at least one member of the public by August 27, 1997. If true, then *Griffiths et al.* and *Pollard* may have been published, and therefore available as prior art, as of that date. *See* M.P.E.P. § 2128.02 (citing *In re Schlittler,* 234 F.2d 882, 110 U.S.P.Q. (BNA) 304 (C.C.P.A. 1956)).

C. The Examiner Improperly Simplifies the Claimed Invention to a "Soul"

The Examiner oversimplifies the claimed invention to consist merely of splitting a batch of cells into two parts. Arguing that "the [soul] of the claimed invention is to divide culturing cells into two parts," the Examiner states that "[c]ompared with dividing culturing cell into more than [two] parts, it [the claimed invention] is a modification of splitting cells in different ratios." Final Office Action at page 3. Moreover, the Examiner demands unexpected results to show the benefit of dividing the cells of the preproduction batch into two parts instead of three parts or five parts. *Id.* at page 4.

This improper oversimplification of the presently claimed invention addresses only section b) of claim 1, which recites "dividing the cells of the preproduction batch into a first part and a second part." The oversimplification ignores sections c) and d), which recite using those parts for at least one production batch and at least one subsequent preproduction batch, respectively. The oversimplification also ignores sections a), e), and f). Appellant's amended claim 1 recites:

> A method for the preparation of cells for use in the production of at least one biological, said method being discontinuous and comprising:
> a) culturing cells to form a preproduction batch,
> b) dividing the cells of the preproduction batch into a first part and a second part,
> c) employing said first part for the preparation of at least one production batch for the production of at least one biological,
> d) employing said second part as a seed for the preparation of at least one subsequent preproduction batch,
> e) optionally culturing the cells of the subsequent preproduction batch to obtain a greater cell population,
> f) optionally repeating b) to e), using the cells of the subsequent preproduction batch of d) or e) for the preproduction batch of b).

Oversimplification of the claimed invention to a "soul" violates the requirement that the claims must be considered as a whole when determining obviousness. *See*

Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861, 874-75, 228 U.S.P.Q. (BNA) 90, 99 (Fed.Cir. 1985), *overruled on other grounds by Nobelpharma AB v. Implant Innovations*, 141 F.3d 1059, 1068, 46 U.S.P.Q.2d 1097, 1104 (Fed. Cir. 1998) (addressing application of Federal Circuit law to antitrust claims). In *Loctite,* the Federal Circuit vacated a district court's finding of obviousness of a process, chastising the lower court for evaluating only the "core" of the claimed process. "[W]hen determining obviousness, there is no legally recognizable or protected 'essential,' 'gist,' or 'heart' of the invention." *Loctite,* 781 F.2d at 875, 228 U.S.P.Q. at 99 (citing *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 721 F.2d 1563, 1567, 220 U.S.P.Q. (BNA) 97, 101 (Fed. Cir. 1983)). Instead, "[d]uring patent examination, the pending claims must be 'given their broadest reasonable interpretation consistent with the specification." M.P.E.P. § 2111 (quoting *In re Hyatt,* 211 F.3d 1367, 1372, 54 U.S.P.Q.2d (BNA) 1664, 1667 (Fed. Cir. 2000)). With this interpretation, the claimed invention must be considered as a whole when determining obviousness. 35 U.S.C. § 103(a) (2000); *see also Medtronic,* 721 F.2d at 1567, 220 U.S.P.Q. at 101.

The Examiner alleges, in the fourth full paragraph on page 3 of the Final Office Action, that Appellant has argued the "sole [sic, soul]" of the invention, referring to Appellant's amendment filed on December 20, 2002. Appellant has done no such thing. In that amendment, Appellant argued that he has invented a new approach to scaling-up a cell culture for production of a biological. *See* Amendment under 37 C.F.R. § 1.111 filed on December 20, 2002, at page 8. This argument should not be misconstrued as Appellant identifying or relying on a "soul" of the claimed invention.

Appellant considers the Examiner's focus on the "soul" of the claimed invention to be the root of the legal error undermining the pending rejections. Appellant

respectfully requests that his claimed invention be considered as a whole, by assigning the claims their broadest reasonable interpretation. *See Medtronic,* 721 F.2d at 1567, 220 U.S.P.Q. at 101.

D. *Prima Facie* Obviousness Does Not Exist Because *Griffiths et al.* and *Pollard* Fail to Teach All Claim Limitations

The Examiner finds Appellant's argument that the cited documents do not teach or suggest all claim limitations to be unpersuasive, "because the cited reference of Griffith et al. and Pollard teach all aspects of scale-up culturing suspension and anchorage dependent cell culture . . . ." Final Office Action at page 3; *see also* Office Action mailed September 20, 2002, at page 4. Appellant respectfully contends that teaching "all aspects of scale-up culturing . . . [of] cell culture[s]" fails to teach all the presently recited claim limitations.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. M.P.E.P. § 2143.

Appellant's amended claim 1 recites, *inter alia*:

> b) dividing the cells of the preproduction batch into a first part and a second part,
> c) employing said first part for the preparation of at least one production batch for the production of at least one biological,
> d) employing said second part as a seed for the preparation of at least one subsequent preproduction batch . . . .

A thorough review of *Griffiths et al.* reveals no discussion of dividing cells into two parts in the manner claimed. When it comes to growing more cells, the cells in *Griffiths et al.* are always used as a single "part" and are never diverted for more than one purpose. *Griffiths et al.* does remove "a small sample" to test for cell viability during the course of culturing. *See Griffiths et al.* at page 63, lines 7-10. The taking of this small sample during culturing, however, does not represent dividing a preproduction batch into two parts for preparing "at least one production batch" and "at least one subsequent preproduction batch." It appears clear that *Griffiths et al.* tests, and then discards, cells taken in the "small sample." *See id.*

Griffiths et al. furthermore describes two approaches to scale-up the population of a cell culture. "The first [approach] is volumetric - a simple increase in volume while retaining the same cell density or process intensity. The second method is to increase the cell density/unit vol 10-100-fold by means of medium perfusion techniques." *Griffiths et al.* at page 60, lines 3-6.

The two approaches of *Griffiths et al.* highlight the inventive nature of Applicant's claimed methods. *Griffiths'* first approach appears in *Wiktor et al.* (U.S. Patent No. 4,664,912), mentioned in Applicant's specification on page 1. (Three copies of *Wiktor et al.* are enclosed for the Board's convenience.) *Wiktor et al.* describes an expansion of preproduction batches from a 1 liter biogenerator up to a 1000 liter biogenerator. *Wiktor et al.* at col. 2, lines 58-69. Only after all preproduction batches have been prepared is the production batch cultured: "the inoculation by the virus [is] effected in this last passage." *Id.* at lines 68-69 (emphasis added). The second approach to scaling-up appears in several places in *Griffiths et al.*, where medium perfusion techniques and equipment are discussed. *See, for example, Griffiths et al.* at page 60, lines 5-13.

Appellant has invented a third approach to scaling up a cell culture population in the context of producing a biological. In Appellant's claimed methods, the skilled artisan cultures subsequent preproduction batches and production batches from the same preproduction batch. In section c) of appealed claim 1, a first part of the preproduction batch is used to prepare "at least one production batch for the production of at least one biological." Claim 1. In section d), the second part of the preproduction batch is used "as a seed for the preparation of at least one subsequent preproduction batch." *Id.; contrast with Wiktor et al.* at col. 2, lines 68-69. No teaching or suggestion of claimed sections c) and d) can be derived from the disclosure of *Griffiths et al.* when considered on its own.

Pollard does not cure the failure of *Griffiths et al.*, either by itself or in combination with *Griffiths et al. Pollard* teaches methods for establishing and maintaining cell cultures and methods for freezing the cells (items 3.1-3.3). On page 2 of the Final Office Action, the Examiner specifically cites steps 14-20 on page 3 of *Pollard.* Those steps relate to the seeding, culturing, and harvesting Chinese hamster fibroblast cultures to establish a primary culture. *Pollard* at page 2. Optionally, subculturing using different split ratios may be used. *Id.* at page 3 (step 20). These steps do not teach or suggest a strategy of culturing cells for the production of a biological; rather, they relate to the establishment of a culture in the first place. *Id.* at page 2. The Examiner also cites Section 3.2 on pages 4-5 of Pollard on page 2 of the Final Office Action. This section details the steps for culturing transformed cells from frozen stock.

Combing through each section of *Pollard* fails to reveal any teaching or suggestion for employing separate parts of the same preproduction batch for production

and subsequent preproduction batches. Thus, *Pollard,* individually or when combined with *Griffiths et al.,* fails to teach or suggest sections c) and d) set forth in claim 1.

This truth is not altered by any of the Examiner's reasoning appearing in prior office actions. In the earliest articulation of the rejection, The Examiner asserted that Appellant's claimed "discontinuous" process represented merely a "design choice" within the disclosure of *Griffiths et al.* as augmented by *Pollard's* teaching of freezing cells. Office Action mailed on August 1, 2001, at page 4. This reasoning shows, at best, that suspending a cell culture by freezing it may have been known. Later, the Examiner asserted that splitting cells in certain ratios and freezing them were within the ordinary skill in the art. Advisory Action mailed on December 3, 2001. Again, and in sum, sections c) and d) of the claims have not been shown.

E. Claim Sections C) and D) Do Not Follow From an Understanding of Split Ratios

The Examiner alleges that Appellant's claimed invention merely represents a modification of split ratios, or dilution, of cells. After discussing the impact of cell density on culturing time, the Examiner characterizes the claimed invention:

> Therefore, it is proper to considering that the claimed invention is regarded as a modification of the splitting cells in different ratios, which is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995) [sic].

Final Office Action at page 3; *see also* Office Action mailed September 20, 2002, at page 4. From this characterization, and given the disclosures of *Griffiths et al.* and *Pollard,* the Examiner concludes that "the discovery of the workable ranges as 1 to 1 or 1 to 2 splitting cells in culture involves only routine skill in the art, In re Aller, 105, USPQ

233." Final Office Action at page 4. Appellant disagrees with this characterization and with the conclusion.

Contrary to the Examiner's characterization, Appellant claims no split ratio. In section b) of claim 1, the cells of the preproduction batch are divided into two parts. This division into "a first part and a second part" (claim 1) contains no information limiting the split ratio, or dilution, at which those cells may be subsequently cultured. These two parts do not require a split ratio of 1:2, or any other split ratio. While modifying a split ratio may be within the ordinary skill in the art, it has no bearing on the claimed invention, and does not teach or suggest the divergent uses of the preproduction batch parts found in claim sections c) and d). The Examiner's continued reference to split ratios belies a fundamental misunderstanding of the claimed invention.

Alleging that *Griffiths et al.* and *Pollard* teach all aspects of scaling-up cell culture, the Examiner also states, "unless the exactly split the preproduction of cell population into two parts, which is noticed by the Office as a modification of splitting cells in different ratios." Final Office Action at page 3. Appellant fails to understand this passage completely. Because it seems to relate to modifying split ratios, Appellant reiterates that an understanding of split ratios does not teach or suggest sections c) and d) of claim 1.

F. The *Prima Facie* Case Also Fails For Lack of Motivation

The *prima facie* case of obviousness also fails, because there is no motivation to modify the teachings of *Griffiths et al.* and *Pollard* to obtain the claimed invention. The Federal Circuit has held that evidence of a teaching, suggestion, or motivation to combine may flow from the cited documents themselves, from the knowledge of one of ordinary skill in the art, or from the nature of the problem, but may not flow from

Applicant's disclosure. *See Pro-Mold and Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996), *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d (BNA) 1438, 1442 (Fed. Cir. 1991). Importantly, this evidence of a teaching, suggestion, or motivation to combine must be "clear and particular." *In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d (BNA) 1614, 1617 (Fed Cir. 1999).

The Examiner seems to find motivation to modify *Griffiths et al.* and *Pollard* to obtain Appellant's claimed methods within the ordinary skill in the art. For example, the Examiner states that "the modification of the splitting cells in different ratios is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995) [sic]." This statement reveals at least two errors in the Examiner's logic. First, the claimed invention does not relate to merely splitting cells in different ratios. Second, the purported invention of *In re Rose* involves bundling lumber, not splitting cells. *See In re Rose,* 105 U.S.P.Q. (BNA) 237, 238 (C.C.P.A. 1955). Regardless of whether modifying cell ratios falls within the abilities of those of ordinary skill, this has no bearing on Appellant's claimed invention.

The Examiner continues the fruitless search for motivation in the alleged prior art: "Because other general conditions for large scale-up culturing . . . cells has bee[n] explicitly disclosed in [*Griffiths et al.* and *Pollard*], the discovering the workable ranges as 1 to 1 or 1 to 2 splitting cells in culture involves only routine skill in the art, In re Aller, 105, USPQ 233." Final Office Action at pages 3-4. Because the claims contain no limitation reasonably construed as "workable ranges as 1 to 1 or 1 to 2 splitting cells in culture," this allegation makes no sense. Moreover, the subject matter of *In re Aller* relates to a method for producing phenol, and does not include "splitting cells in culture."

See In re Aller, 105 U.S.P.Q. (BNA) 233, 234 (C.C.P.A. 1955). Accordingly, *In re Aller* offers no support for the Examiner's proposition.

Nonetheless, the Examiner clearly means to rest the motivation in the ordinary skill in the art. For example, the Examiner stated that "because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the workable ranges involves only routine skill in the art[.]" Office Action mailed September 20, 2002, at page 4. Similarly, "Therefore, in order to continuously produce a biological molecule from a biological characteristic consistent cell line, the motivation for combining the cell spitting and cell frozen technique would have been obvious for an ordinary skill in the art." Advisory Action mailed on December 3, 2001, at page 3.

The Examiner has not shown how Appellant's claimed invention involves merely discovering workable ranges of general methods taught or suggested in the alleged prior art. As discussed above, The Examiner has not shown claim sections c) and d) in any teaching in the cited documents. It follows that the motivation to modify the alleged prior art to create sections c) and d) cannot be found in the alleged prior art, either. As a matter of law, it is improper to leap over this fatal gap in the *prima facie* case by resorting to ordinary skill in the art. "The level of skill in the art cannot be relied upon to provide the suggestion to combine references." M.P.E.P. § 2143.01 (citing *Al-Site Corp. v. VSI Int'l Inc.,* 174 F.3d 1308, 50 U.S.P.Q.2d 1161 (Fed. Cir. 1999)). Accordingly, Appellant submits that the examiner has failed to show motivation to modify the teachings of *Griffiths et al.* and *Pollard* to make Appellant's claimed invention.

Appellant submits that the Examiner has not met the burden of providing "clear and particular" evidence in the cited documents, the knowledge of one of ordinary skill

in the art, or in the nature of the problem, to show motivation to obtain Appellant's claimed methods.

IX. Conclusion

At least because the Examiner has not met the burden for showing that all claim limitations have been taught or suggested, or that the requisite motivation exists with clear and particular evidence, Appellant respectfully requests that this rejection be reversed for a failure of the *prima facie* case of obviousness, and claims 1, 2, and 7-25 be allowed to issue.

Appellants file herewith a Petition for Extension of Time (Five Months) and fee therefor. If any further extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, Appellants respectfully request such extension. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 that are not enclosed herewith, including any fees required for any extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: January 9, 2004

By: _____
Jeremy M. Stipkala
Reg. No. 44,359

Post Office Address (to which correspondence is to be sent)

Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, D.C. 20005
(202) 408-4000

Enclosures:
Appendix A (Claims after Amendment filed December 20, 2002)
Wiktor et al. (U.S. Patent No. 4,664,912)

APPENDIX A

Pending claims 1, 2, and 7-26, following entry of the December 30, 2002, Amendment, appear listed below.

1. (Thrice amended) A method for the preparation of cells for use in the production of at least one biological, said method being discontinuous and comprising:

a) culturing cells to form a preproduction batch,

b) dividing the cells of the preproduction batch into a first part and a second part,

c) employing said first part for the preparation of at least one production batch for the production of at least one biological,

d) employing said second part as a seed for the preparation of at least one subsequent preproduction batch,

e) optionally culturing the cells of the subsequent preproduction batch to obtain a greater cell population,

f) optionally repeating b) to e), using the cells of the subsequent preproduction batch of d) or e) for the preproduction batch of b).

2. (Thrice amended) The method according to Claim 1 wherein:

a) said first part is transferred for the preparation of the at least one production batch, and

b) said second part is transferred to be used as a seed for the preparation of the at least one subsequent preproduction batch.

7. The method according to Claim 1, wherein a first preproduction batch is prepared from a working seed stock by at least one passage part.

8. The method according to Claim 2, wherein a first preproduction batch is prepared from a working seed stock by at least one passage part.

9. The method according to Claim 1, wherein the cells are anchorage dependent.

10. (Twice Amended). The method according to Claim 9, wherein the anchorage dependent cells are derived from hamsters, monkeys, bovines, canines, humans, or chickens.

11. The method according to Claim 2, wherein the cells are anchorage dependent, are grown on a substrate, and are released from said substrate prior to each transfer part.

12. The method according to Claim 11, wherein the substrate comprises particulate matter or a solid support.

13. The method according to Claim 12, wherein the solid support comprises hollow fibers or micro-carriers or macro-carriers in suspension.

14. The method according to Claim 11, wherein the cells are embedded in a carrier.

15. The method according to Claim 14, wherein the carrier is a Cytodex-3 micro-carrier.

16. The method according to Claim 11, wherein the cells are released from said substrate with a proteolytic enzyme.

17. The method according to Claim 16, wherein the proteolytic enzyme is trypsin.

18. The method according to Claim 16, wherein the cells are treated with PBS and/or EDTA prior to exposure to the proteolytic enzyme.

19. The method according to Claim 1, wherein the biological is a virus.

20. The method according to Claim 1, wherein the biological is a protein.

21. The method according to Claim 20, wherein the protein is an enzyme.

22. (Once amended) The method according to Claim 1, wherein:

a) the proportion of the cells of the preproduction batch forming said first part ranges from 80% to 90%, and

b) the proportion of the cells of the preproduction batch forming said second part ranges from 10% to 20%.

23. The method according to Claim 1, wherein the cells are parked at a certain passage number by exposure to an ambient temperature ranging from 17 to 32 degrees C.

24. The method according to Claim 23, wherein said parked cells are revitalised to log growth by raising the temperature and changing the culture media.

25. (Once Amended). The method according to Claim 1, wherein the cells are frozen at a temperature of less than -80 degrees C in bulk, and thawed prior to use.

26. The method according to Claim 10, wherein:

a) the cells derived from hamsters are CHO or BHK-1 cells;

b) the cells derived from monkeys are Vero cells;

c) the cells derived from bovines are MDBK cells;

d) the cells derived from canines are MDCK cells;

e) the cells derived from humans are CaCo or A431 cells; or

f) the cells derived from chickens are CEF cells.